

**REMARKS**

Claims 1-29 are currently pending. Claims 8-25 and 27-29 are withdrawn from consideration. Claims 1-7 and 26 are examined on the merits. Claim 1 and claim 7 are amended herein. Support for the amendments to claim 1 may be found throughout the Specification, e.g., at page 4, line 4 to page 5, line 9, in claim 4 as previously presented, and in the Examples and Figures. No new matter has been added. Claim 4 is cancelled herein. Entry of the amendment is respectfully requested.

**Rejections Under 35 U.S.C. § 112, Second Paragraph:**

Claims 1-7 and 26 have been rejected under 35 U.S.C. § 112, second paragraph as being indefinite. In view of the amendments made herein to claim 1, the rejection is now moot.

**Rejections Under 35 U.S.C. § 112, First Paragraph:**

Claims 1-7 and 26 have been rejected under 35 U.S.C. § 112, first paragraph for lacking enablement. In response, Applicants have amended claim 1 herein to specify that the marker protein is a fusion protein containing a fluorescent fragment. Applicants respectfully submit that the specification clearly teaches methods of the present invention wherein the marker protein is a fusion protein comprising a fluorescent fragment, including not only the chimeric protein GFP-BAX, but also the fluorescent proteins DsRed, HcRed and copGFP (see, e.g., Example 1, Example 3, Figure 8 and Figure 12). In view of the amendments made herein to claim 1, the rejection is now moot.

**Rejections Under 35 U.S.C. § 102:**

Claims 1-7 and 26 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Wolter et al., *J. Cell Biology*, Vol. 139, No. 5, Dec. 1, 1997, pp. 1281-1292 ("Wolter").

According to the Examiner, *Wolter* anticipates the claimed invention as it allegedly teaches a method for the demonstration of an apoptotic event in a cell comprising the binding of solubilized marker protein, such as GFP fused to Bax, Bcl-2 and Bcl-X<sub>L</sub>, which is a direct marker for the occurrence of an apoptotic event, where the marker protein is present in the cell before the detection; and the presence of the marker protein being detected in the cell by an appropriate means including fluorescence microscopy, which makes it possible to determine whether binding and thus apoptotic event has occurred. Applicants respectfully traverse.

In response, Applicants respectfully submit that *Wolter* relates to the visualization of cellular distribution of Bax during apoptosis by using a fusion protein (GFP-Bax) and analysis of confocal images in living cells. In cells undergoing apoptosis, the fluorescent signal is redistributed from the cytosol to the mitochondria. *Wolter*, however, does not disclose a method for the demonstration of the occurrence of a specific molecular event in a cell wherein the cell is subjected to a permeabilization of the plasma membrane before the detection of a protein marker. Applicants respectfully submit that as this permeabilization step is not disclosed in *Wolter*, the cited reference does not disclose every element of the Applicants' claimed method, and thus the instant invention is novel in view of *Wolter*. Thus, Applicants respectfully request that the rejection of claims 1-7 and 26 under 35 U.S.C. § 102(b) be withdrawn.

As it is believed that all of the rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he telephone Applicants' attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

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Respectfully submitted,  
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